

### **REMARKS**

Claims 56-68 and 78-86 are pending. Claims 56, 58, and 78 are amended. Claims 1-55, 69-77, and 87-117 are cancelled. Claims 118 and 119 are added. The amendments to the claims find support in the specification as filed. No new matter is added.

Applicants note that claims 56-68 and 78-86 were previously found allowable by Examiner Tran. While Applicants acknowledge that new art was cited by Applicants, thus, giving rise to the §102 and 103 rejections below, the remainder of the rejections set forth in the Office Action appear to be inappropriate. The MPEP states at section 706.04 that, with respect to previously allowed claims, "full faith and credit should be given to the search and action of a previous examiner unless there is clear error in the previous action...in general, and examiner should not take an entirely new approach or attempt to reorient the point of view of the previous examiner." In particular, with respect to the rejections currently raised under §112, second paragraph, and the §102 rejection in view of Rowe et al., these issues were fully prosecuted previously (or, in the case of Rowe et al., the prior examiner was made aware of Rowe et al. and did not make a rejection) and the now rejected claims were deemed to be allowable over the prior prosecution. The Examiner has not provided any rationale as to why the claims are now being rejected anew, when no changes to the claim language has been made since the claims were determined to be allowable. Accordingly, Applicants request at the outset that the instant rejections not precipitated by Applicants IDS filing of 8/17/07 be withdrawn as previously overcome by Applicants.

### **Objection to the Specification**

The Office Action states that the specification is objected to for failing to provide proper antecedent basis for the terms "control sequence," "operatively linked," and "naked or complexed nucleic acid." Applicants disagree and traverse the rejection.

It is well established that the original claims of an application constitute part of the disclosure of the invention. See, MPEP 608.01(I). The terms "operatively linked"

and “control sequences” were both recited in original claim 18. In addition, the term “naked or complexed nucleic acid” was present in original claim 24. Thus, these terms were part of the original disclosure of the application and, therefore Applicants request that the rejection be reconsidered and withdrawn.

**Rejection of Claims 56-68, and 78-86 Under 35 U.S.C. §112, First Paragraph**

The Office Action states that claims 56-68 and 78-86 are rejected under §112, first paragraph as failing to comply with the written description requirement. The Office Action states that the specification does not provide sufficient written description for a first and second repertoire, each comprising a heavy or light chain polypeptide. The Office Action states that the specification does not provide support for the genus of heavy or light chain polypeptides. Applicants disagree and traverse the rejection.

The specification teaches first and second repertoires on page 1, lines 10-13, which refers to a first repertoire and a second repertoire and also to a repertoire of heavy chains and a repertoire of light chains. Page 6, lines 24-25 also refers to a repertoire of heavy chains and a repertoire of light chains, and page 2, lines 25-26 describes screening a first repertoire of molecules against a second repertoire of molecules. Thus, the specification provides ample support for the claims as written. Moreover, as noted above the claims were previously found to be allowable, and the Examiner has provided no rationale for why the description of the invention, previously held allowable under §112, first paragraph is now rejected.

Notwithstanding the foregoing, and without acquiescing to the rejection, and solely to expedite the prosecution in this case, Applicants have amended the claims to recite an “antibody heavy chain” or “antibody light chain.” Indeed the Office Action acknowledges that the specification discloses heavy and light chains of antibodies. Accordingly, Applicants request that the rejection be reconsidered and withdrawn.

**Rejection of Claims 56-68 and 78-86 Under 35 U.S.C. §112, Second Paragraph**

The Office Action states that the term “continuous line” in claim 56, 57, 63, 67, and 68 is a relative term that renders the claim indefinite, and that one of skill in the art would not be reasonably appraised of its scope. The Office Action quotes several passages, allegedly from the instant specification, to support the rejection. The quoted text, however, does not appear in the instant specification. Applicants assume that the Examiner is quoting passages from the copending CIP application 10/008,571.

As noted above, the instant claims, including recitation of “continuous line”, “juxtaposed,” and the various recitations of heavy and light chain, were found to be allowable by Examiner Tran. The Office Action has provided no explanation of why the terms recited in the allowed claims are suddenly vague and indefinite. To the extent that the rejection is maintained, Applicants request that the Examiner provide an explanation of why, as required by the MPEP, full faith and credit is not being afforded to the prior examination by Examiner Tran.

It is well understood that during patent examination, the pending claims must be given their broadest reasonable interpretation consistent with the specification. *In re Hyatt*, 211 F.3d 1367, 1372, 54 USPQ2d 1664, 1667 (Fed. Cir. 2000). The interpretation given a particular claim term or phrase must be consistent with the interpretation that one of ordinary skill in the art would reach. *In re Cortright*, 165 F.3d 1353, 1359, 49 USPQ2d 1464, 1468 (Fed. Cir. 1999). Moreover, the law is clear that the standard for determining definitiveness is whether one of skill in the art would understand what is claimed. *Amgen v. Chugi*, 927 F.2d 1200 (C.A. Fed. 1991). Definitiveness is determined, in part, from a reading of the specification. *Texas Instruments, Inc. v. U.S. Intern. Trade Com'n*, 871 F.2d 1054 (C.A. Fed. 1989).

With respect to the instant specification and claims, given the general knowledge in the art and the disclosure of the specification, one of skill in the art would clearly discern the scope of the claimed “continuous line.” The specification describes at page 3, second paragraph, that juxtaposition can be arrived at by “creating a series of lines for each of the two repertoires.” The specification teaches at page 12 that dispensing events can include creating a “single continuous line of liquid.” The

specification teaches further at page 3, second paragraph, ways in which continuous lines can be configured: “[t]he lines can be straight, substantially parallel lines, or curves, or combinations thereof; the only restriction is that all members of the first repertoire should be able to interact [with] all members of the second repertoire...configurations include straight parallel lines, disposed at an angle to straight parallel lines; concentric circles or polygons, used together with a star or radial lines.” Moreover, the specification teaches working examples of making a first and second series of continuous lines; see, for example, Figures 1 and 2. In addition, the specification provides working examples showing the creation and arranging of a first and second repertoire in a first and second series of continuous lines (see examples 1 and 2). Thus, one of skill in the art would have clearly understood what is encompassed by the term “continuous line.”

The Office Action states that the term “juxtaposed” in claims 56, 62, 67, and 67 (“juxtaposing”) is a relative term that renders the claim indefinite. Applicants disagree and traverse the rejection.

With respect to the term “juxtaposed”, the specification states on page 11, that juxtaposed refers to a spatial arrangement of members of the first and second repertoire such that “molecules are *capable of interacting with one another* in such a manner that the sites of interactions between the members of the repertoires can be correlated with their position.” The claims require that a plurality of the first series of lines interacts with a plurality of the second series of lines, wherein a plurality of members of the first repertoire are juxtaposed with members of the second repertoire. This is clear and unambiguous, and one of skill in the art would readily understand the metes and bounds of the claimed invention. The Office Action has, again, cited passages, allegedly from the specification, to support the rejection. These passages, however, do not appear in the instant specification. One of skill in the art would understand the meaning of juxtaposed, given the knowledge and skill in the art, coupled with the teachings in the specification.

The Office action states that the limitation “a heavy or light chain polypeptide” in claim 56 is unclear as there is “uncertain antecedent basis.” Applicants disagree. The claim is clear in that it encompasses a first and second repertoire, each comprising an antibody heavy or light chain. The claim allows for the antibody heavy or light chains of the first and second repertoire to be the same or different. There is no ambiguity in the claim.

The Office Action states that the terms “heavy” and “light” in claim 56 are indefinite as they are relative terms and there is not standard to ascertain the “heaviness” or “lightness” of the polypeptides. The claims have been amended to recite an antibody heavy chain or antibody light chain. These are terms well known to those of skill in the art, and one of skill in the art would immediately recognize that there is no ambiguity as to the “heaviness” or “lightness” of an antibody heavy or light chain.

The Office Action states that the term “said heavy or light chain” in claim 58 is indefinite because it is unclear which heavy or light chain is being referred to: that of the first repertoire or second repertoire. Claim 58 has been amended to clarify that the claim refers to the antibody heavy or light chain of either the first or second repertoire.

The Office Action states that claim 64 is indefinite in the recitation of “a different target antigen.” The Office Action states that the antecedent basis of this term is unclear because it is unclear what the target antigen is different from. Claim 64 has been amended to clarify that with respect to the third repertoire, the target antigen in one line is different with respect to a target antigen in another line of the third repertoire.

The Office Action states that claim 78 is rejected with respect to the term “if present, third repertoires, and “said target epitope.” Claim 78 has been amended and new claims 118 and 119 added to clarify the scope of the claimed invention.

In view of the foregoing, Applicants believe that the claims are clear and unambiguous and request that the rejections be reconsidered and withdrawn.

**Rejection of Claims 56-61, 65-68, 78, 79, and 83 Under 35 U.S.C. §102(b)**

*Biebuyck et al.*

The Office Action states that claims 56-61, 65-68, 78, 79, and 83 are rejected under §102(b) as allegedly anticipated by Biebuyck et al. The Office Action states that Biebuyck et al. teaches a method of immobilizing chemically defined bodies (CDBs). The Office Action quotes a passage of Biebuyck et al. that teaches the patterning of complementary CDBs (C-CDBs) via a series of parallel channels oriented orthogonal to each other. The Office Action concludes that this anticipates the claimed invention. Applicants disagree and traverse the rejection.

It is well settled law that to anticipate a claim, a prior art reference must teach, either expressly or inherently, each element of the claimed invention. *See, e.g., Perricone v. Medicis Pharmaceutical Corp.*, 432 F.3d 1368 (Fed. Cir. 2005). Biebuyck et al. does not anticipate the claimed invention because it does not teach each element recited by the claims.

The instant claims relate to a method of screening a first repertoire of an antibody heavy chain or antibody light chain against a second repertoire of an antibody heavy chain or antibody light chain to identify those members of the first repertoire which interact with members of the second repertoire. Biebuyck et al. relates to receptor/ligand screening, and thus, regardless of the method used to juxtapose the members of the repertoires, Biebuyck et al. do not teach a method for screening repertoires of antibody heavy or light chain polypeptides. Not only is there no teaching in Biebuyck et al. of screening for interactions between repertoires of antibody heavy or light chain molecules, but Biebuyck et al. is silent as to screening for interactions between any antibody or fragment thereof. Thus, Biebuyck et al. does not teach each element of the claimed invention and does not anticipate the instant claims.

*Rowe et al.*

The Office Action states that claims 56-58, 60, 62-68, 78, and 79 are rejected as anticipated by Rowe et al. The Office Action states that Rowe et al. teach methods of producing two-chain or three-chain polypeptides comprising utilizing an array

immunosensor wherein vertical channels comprise antibodies labeled with biotin and adding samples flowed through horizontal channels. Applicants disagree and traverse the rejection.

Rowe et al. does not teach or suggest a method of screening for an interaction between two repertoires of antibody heavy or light chains. While Rowe et al. teaches patterning of three specifically selected capture antibodies in vertical "stripes" on a surface, Rowe et al. does not teach a first or second repertoire of antibody heavy or light chains. Rowe et al. teaches that the antibodies are screened against blood samples, saliva, urine, serum, plasma, and nasal secretions. These physiological samples are heterogeneous in nature and do not equate to a repertoire of antibody heavy or light chains as required by the instant claims. Thus, Rowe et al. does not teach a method for screening for the interaction of members of a first and second repertoire of antibody heavy or light chains.

**Rejection of Claims 56-68 and 78-85 Under 35 U.S.C. §103(a)**

The Office Action states that claims 56-68 and 78-85 are rejected under §103(a) as unpatentable over either Biebuyck et al. or Rowe et al. in view of Buechler et al. The Office Action applies Biebuyck et al. and Rowe et al. as noted above, but states that neither reference teaches a first repertoire of V<sub>H</sub> and a second repertoire comprising V<sub>L</sub>, and do not teach methods comprising nucleic acid sequences, expression vectors and host cells. The Office Action states that Buechler et al. teach a method of producing a multivalent polypeptide display library. The Office Action states that Buechler et al. teaches a method of constructing libraries of antibody fragments comprising light or heavy chain for screening. The Office Action states that one of skill in the art would have been motivated to make and use methods comprising a first repertoire comprising V<sub>H</sub> and a second repertoire comprising V<sub>L</sub>, because it would have been desirable to produce expression libraries or antibodies and/or their variable regions for affinity screening, to achieve diverse populations. Applicants disagree and traverse the rejection.

Buechler teaches methods for the production of multivalent polypeptide display libraries. Buechler teaches that a double chain antibody library may be generated by fusing one antibody chain to a phage coat protein, and then fusing a partner antibody chain to the first antibody chain, thus forming a Fab fragment which may be screened for antigen binding properties (col. 2, lines 35-45; col. 10, lines 8-14). Buechler, however, *does not teach that either chain of a double chain antibody library may be applied in the form of an array*, and moreover, *does not teach that any member of an antibody library is arranged in a series of continuous lines*. It would not have been obvious to one of skill in the art to modify the teachings of Buechler et al., which are based on phage-based screening assays, to instead use the immunosensor method of Rowe et al. to arrive at the claimed invention.

Indeed, Rowe as mentioned above describes an immunoassay performed using an immunosensor. In this immunoassay three specific chosen antibodies for detection are labeled with biotin for immobilization to the sensor surface. These are then used to screen samples for the presence of three different analytes. As noted above, Rowe et al. does not teach screening repertoires of molecules, and does not teach or even suggest repertoires of antibody heavy or light chains.

It is well settled that if the proposed modification or combination of the prior art would change the principle of operation of the prior art being modified, then the teachings of the references are not sufficient to render the claims obvious. MPEP §2140.01(VI). As described above, the method of Rowe et al. relates to immunosensor assays wherein a capture antibody placed on a solid surface is screened against a biological patient sample to determine analyte binding. To modify the teachings of Rowe et al. based on the teachings of Buechler et al. would change the principle of operation of Rowe et al. That is, the methods of Buechler et al. would not permit the successful application of the immunoassay methods of Rowe et al.

Hence the skilled person reading Buechler in combination with Rowe would still not have been motivated to produce repertoires of antibody heavy or light chains

and to simultaneously screen each member of one repertoire against each member of the other repertoire, as is specified in the present claims.

With respect to the combination of Buechler et al. and Biebuyck et al., the claims are likewise not obvious over the combination of references. The only teachings in Biebuyck et al. relating to the use of a patterning device “with parallel channels each which are oriented orthogonal to each other” relates to the simultaneous deposition of complementary chemically defined bodies “in particular ligands or receptors.” That is, Biebuyck et al. teaches patterning of “complementary molecules” and does not teach or suggest the patterning of antibody heavy or light chains, which are not “complementary” molecules based on the teachings of Biebuyck et al. Thus, one of skill in the art would not have been motivated based on the teachings of Biebuyck et al. to modify such teachings to instead be employed with the antibody molecules of Buechler et al.

Moreover, as noted above a finding of obviousness cannot be sustained when the combination of the prior art would require a change in the biological operation of the prior art. Again, the teachings of Biebuyck et al. regarding to orthogonally arranged sets of parallel lines relates only to patterning of complementary chemically defined bodies. To change the teachings of Biebuyck et al. to use, instead, the antibody molecules of Buechler et al. would alter the principle of operation of Biebuyck et al. Accordingly, the teachings of Biebuyck et al. and Buechler et al., whether considered alone or in combination would not render the instant claim obvious.

Accordingly, Applicants request that the rejection be reconsidered and withdrawn.

**Rejection of Claim 86 Under 35 U.S.C. §103(a)**

The Office Action states that claim 86 is rejected as being unpatentable over the teachings of Biebuyck et al., or Rowe et al. in view of Buechler et al. and further in view of Bussow et al. The Office Action applies Biebuyck et al., Rowe et al. and Buechler et al. as noted above, and states that Bussow et al. teaches a picking/gridding robot that gridded onto filter membranes cell expressing proteins and then adding a

“stream” of monoclonal antibody. The Office Action concludes that it would have been obvious for one of skill in the art to have made and used methods comprising arraying at least one repertoire using robotic means. Applicants disagree and traverse the rejection.

As discussed above, the invention recited in the pending claims (including claim 86) is not obvious in view of Biebuyck et al., or Rowe et al., in view of Buechler et al. Bussow et al. is being relied on only to the extent that it teaches arraying by robotic means. The teachings of Bussow et al. do not provide the elements of a *prima facie* case of obviousness missing from the combination of Biebuyck et al., or Rowe et al., in view of Buechler et al. Moreover, Bussow et al. does not teach or even suggest arranging a first and second repertoire of antibody heavy or light chains in a first and second series of continuous lines. The teachings of Bussow et al. are limited to gridding of bacterial colonies on a surface. The figure legend for Figure 1 states that gridding patterns of 3x3 or 5x5 were used; that is a pattern of 3x3 spots or 5x5 spots. Thus, when referring to “gridding” Bussow et al. is referring to spotting onto a surface, not depositing bacterial colonies (or anything else) in a series of continuous lines. In addition to failing to teach arranging a first repertoire of antibody heavy or light chains in a first series of continuous lines, there is no teaching in Bussow et al. of depositing a second repertoire of antibody heavy or light chains in a second series of continuous lines such that the lines of the first series intersect with the lines of the second series. Thus, Bussow et al. adds nothing to the teachings of Biebuyck et al., or Rowe et al., in view of Buechler et al. to support a finding of obviousness.

Because the teachings of Biebuyck et al., or Rowe et al., in view of Buechler et al. do not render the base invention obvious, the addition of Bussow et al. does not render claim 86 obvious. Accordingly, Applicants request that the rejection be reconsidered and withdrawn.

In view of the above amendment, applicant believes the pending application is in condition for allowance.

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